[JP,05-148151,A]

[Claim(s)]

[Claim 1] The filter ingredient for transfusion for removing a leucocyte from the whole blood or erythrocyte pharmaceutical preparation which consists of a macromolecule porous body which has a nonwoven fabric, textile fabrics, or continuation pore, and is characterized by having one or more sorts of acid functional groups on a front face.

[Detailed Description of the Invention]

[0001]

[Industrial Application] This invention relates to the filter ingredient for leukopheresis. In detail, it is related with the filter ingredient for removing a mixing leucocyte from the whole blood for transfusion, or erythrocyte pharmaceutical preparation.

[0002]

[Description of the Prior Art] In recent years, in the transfusion field, the so-called leukopheresis transfusion which removes and transfuses the mixing leucocyte contained in a blood product is performed increasingly. This is because it became clear that the leucocyte which critical side effects, such as side effects, such as a headache accompanying transfusion, nausea, a chill, and nonhemolytic exothermic reaction, and after [GVHD] the alloantigen sensitization which has more serious effect on a recipient, and transfusion, a viral infection, are mixing into the blood product mainly used for transfusion is caused owing to.

[0003] In order to prevent comparatively slight side effects, such as a headache, nausea, a chill, and fever, it is supposed by one transfusion that it is necessary to hold down the white blood cell count poured into a recipient to about 100 million or less pieces, and for that, it is necessary to remove the survival rate of the leucocyte in a blood product until it becomes 10-1 to ten to two or less. Moreover, it is required to remove until alloantigen sensitization attracts attention most in the current transfusion study field, and is supposed that it is necessary to hold down the white blood cell count poured in by one transfusion to 5 million pieces or 1 million pieces or less in order to prevent this, although it is one of the side effects that that prevention is expected and for that it becomes ten to four or less about the survival rate of the leucocyte in a blood product. Although there is still no established theory about the transfusion back GVHD and a viral infection, like after [GVHD] transfusion and a cytomegalovirus, or an adult-T-cell-leukemia virus, about the virus considered to exist only in a leucocyte, it is removing to 10-4 to ten to six or less leucocyte survival rate, and it is expected that the infection can be prevented. Moreover, it is expected

like HIV also about the virus which exists in both a leucocyte and plasma that the frequency of infection may be lowered by leukopheresis.

[0004] Although there are two kinds of approaches of removing a leucocyte from a blood product, the approach of dividing roughly and separating using the difference in the specific gravity of an erythrocyte and a leucocyte using a centrifugal separator and the filter method for removing a leucocyte using the filter which uses fibrin material and the sponge-like structure as a filtering medium Since it has advantages, like that the filter method which carries out adsorption treatment of the leucocyte using a nonwoven fabric especially is excellent in leukocyte removal capability, that actuation is simple, and cost is low, it is used widely.

[0005] Most leukopheresis filters using a nonwoven fabric consist of two kinds of functionally different filter elements, the pre-filter for removing an aggregate with a comparatively coarse eye whose average fiber diameter is about 3-30 micrometers, and the main filter for removing the leucocyte which an average fiber diameter becomes from the fiber which is about 1-3 micrometers. Among these, the pre-filter is made desirable [what has composition of a multistage story to the thing with the thing with a thick average fiber diameter which has a coarse eye to a comparatively thin average fiber diameter which has a fine eye] in order toward a blood inlet port to the blood outlet (JP,2-13588,B, W089 / No. 03717).

[0006] An aggregate is what was able to condense and do cell components, such as a denaturation component of blood, such as a fibrinogen, a fibrin, denatured protein, a nucleic acid, and a lipid globule, and a leucocyte, a platelet, is rich in adhesiveness, and has the very large distribution whose size of the also exceeds 1mm depending on several micrometers to 100 micrometers, and the case. Therefore, it is necessary to remove an one by one more small aggregate by catching and removing a big aggregate with a filter with a coarse eye first, and making the eye fine gradually so that a screen may separate a particle. In the layer with the finest eye of the pre-filter used in order to remove a small aggregate, although some leucocytes may be caught secondarily so to speak, it is **** part, and in order to remove a leucocyte, the main filter described below must be used.

[0007] A diameter is 5-20 micrometers, and the leucocyte which is the main removal purpose has far uniform size as compared with the aggregate, and is considered that the removal device with a filter is the adsorption treatment by fiber. this invention person etc. has found out that the leucocyte concentration which passes fiber laminated material previously decreases exponentially to the thickness of fiber laminated material (JP,3-158168,A), and in case the leucocyte flows fiber laminated

material in the thickness direction, whenever this contacts near the confounding point of fiber and fiber, it suggests adsorb by the fixed probability and has supported the above-mentioned adsorption treatment theory.

[0008] So, there was little what was concentrating examination of high-performance-izing of the main filter in the conventional leukopheresis filter on raising the contact frequency of fiber and a leucocyte chiefly, i.e., making an average fiber diameter small, raising pack density, using the nonwoven fabric which has more uniform fiber diameter distribution (JP,2-203909,A), etc., and observed the chemical property on the front face of a nonwoven fabric.

[0009] As a few examples of examination which paid their attention to the chemical property on the front face of a nonwoven fabric, although there are JP,1-249063,A, a Patent Publication table No. 502094 [three to], etc. It is the purpose of surface treatment that the former raises the permeability of a platelet, the latter gives a hydrophilic property and the purpose makes the priming by blood easy. There are not all and a publication that the adsorption probability of raise [the adsorption probability of a leucocyte] of a leucocyte improved not by the purposes but by these surface chemistry qualification, either.
 [0010] Moreover, if the polymer in which it is indicated in the example that the elimination factor of a leucocyte also increases by the approach of coating W087 / No. 05812 with the polymer which contains the basic functional group and nonionic hydrophilic group of the amount of optima in a nonwoven fabric at the same time the permeability of a platelet increases, and it contains more basic functional groups is used, it is indicated by the example of a comparison that an elimination factor increases in a platelet and a leucocyte. If the front face of a cell considers having negative charge generally, between the basic functional group which has positive charge under physiological conditions, and the negative charge of cell surface, it will be thought of for ion-bonding strength to work by the polymer which has a basic functional group that the elimination factor of a leucocyte increases, and it will be considered to be a very appropriate result.

[0011] Moreover, the individual matter of the water-insoluble nature which has a carboxyl group as a technique of separating ****** of a leucocyte (JP,55-136230,A), Although the water-insoluble nature individual matter (JP,55-149839,A) containing an acid functional group, the granular hydrophobic individual matter (JP,56-152740,A) containing an acid functional group, etc. are indicated Here, the acid functional group is used as what lowers adsorbent [of the specific groupoid in a leucocyte], are collected, without making this groupoid adsorb according to this operation, and aim at separating the cell population to which adsorbent does not fall by existence of an acid

functional group, either, and the above-mentioned groupoid.

[0012]

[Problem(s) to be Solved by the Invention] however, in a nonwoven fabric, textile fabrics, or the filter ingredient for leukopheresis using a macromolecule porous body, a filter ingredient front face is chemical -- there was nothing that examined completely what kind of effect description would have on the adsorption probability of a leucocyte. The purpose of this invention is by giving fixed chemical property to these ingredients front face in offering the high filter ingredient of the leukocyte-removal-capability force, and the filter ingredient for leukopheresis which consists of a nonwoven fabric, textile fabrics, a macromolecule porous body, etc. in more detail to offer a filter ingredient with the more high leukocyte-removal-capability force.

[0013]

[Means for Solving the Problem] When an acid functional group was introduced into it being completely unexpected as a result of making a nonwoven fabric front face carry out direct polymerization and examining the effectiveness of these surface qualification by the radiation graft method that the above-mentioned purpose should be attained on a nonwoven fabric front face, this invention person etc. finds out that the improvement effect of clear leukocyte removal capability is acquired compared with installation before, and came to complete this invention. That is, it is a filter ingredient for transfusion for removing a leucocyte from the whole blood or erythrocyte pharmaceutical preparation which this invention consists of a macromolecule porous body which has a nonwoven fabric, textile fabrics, or continuation pore, and is characterized by having one or more sorts of acid functional groups on a front face.

[0014] Although the charge of a filter material in this invention may be which gestalt of well-known charges of a filter material, such as paper besides the nonwoven fabric created by the melt blowing method, a flash plate spinning method or the milling-paper method, etc., textile fabrics, a mesh, and a porous body, a nonwoven fabric is an especially suitable gestalt. In addition, a nonwoven fabric means the blanket-like thing by knitting and weaving combined chemically, thermally [the aggregate of fiber or yarn], or mechanically ** here. When the fixed configuration is being maintained friction by fiber and fiber contacting mutually, by tangling each other, etc., it includes in having been combined mechanically.

[0015] Moreover, if the example of fibrin material is given, they will be regenerated fibers, such as synthetic fibers, such as a polyamide, aromatic polyamide, polyester, a polyacrylonitrile, poly trifluoro chloroethylene, polymethylmethacrylate, polystyrene,

polyethylene, and polypropylene, and a cellulose, cellulose acetate, etc.

[0016] It is more desirable that the average fiber diameter is 0.3-10 micrometers, as for the filter ingredient of this invention which consists of a nonwoven fabric and textile fabrics, it is more desirable that it is 0.3-3 micrometers, and it is more desirable that it is further 0.5-1.8 micrometers. Since the contact probability of fiber and a leucocyte is too low when an average fiber diameter is less than 0.3 micrometers, the pressure loss at the time of filtering whole blood and erythrocyte pharmaceutical preparation is too high, there is fear which is not practical and 10 micrometers is exceeded conversely, it is for a possibility that the effectiveness of this invention may not fully be demonstrated to become strong.

[0017] In addition, an average fiber diameter means the value calculated according to the following procedures here. That is, a part of filter element substantially accepted to be homogeneity from the nonwoven fabric of one sheet which constitutes a filter element, or two or more sheets, or textile fabrics is sampled, and it photographs in a photograph using a scanning electron microscope etc. On the occasion of a sampling, a filter element is classified with the square whose one side is 0.5cm, and random sampling of the six places is carried out from the inside. What is necessary is just to choose the partition of a need KA place by using a table of random numbers etc., after specifying an address as each above-mentioned partition in order to carry out random sampling for example. Moreover, three partitions of the remainder [partitions / which were sampled first / three / field / (it is called the Ath page below for convenience) / one] photograph the central part by one 2500 times the magnifying power of this in a photograph about the field (it is called the Bth page below for convenience) of another side. A photograph is taken until the sum total number of the fiber which takes the photograph of the part of a central part and its near about each sampled partition, and was photographed by the photograph exceeds 100 and the number turns into a small number most. Thus, the diameter of all the reflected fiber is measured about the acquired photograph. A diameter means the width of face of the fiber of the direction of a right angle to a fiber axis here. Let the value which divided the sum of the diameter of all the measured fiber by the number of fiber be an average diameter. However, two or more fiber overlaps, and in **, these data are deleted when the fiber from which a diameter differs still more remarkably when it becomes the shade of other fiber and the width of face cannot be measured, and when two or more fiber fuses and it has become thick fiber is intermingled. Moreover, when an average fiber diameter differs from the Ath page clearly by the Bth page, this is not accepted to be a single filter element any longer. The case where a significant difference is

statistically accepted "Average fiber diameters differ clearly" here is said. In this case, an Ath page and Bth page side is regarded as a different filter element, and after finding both interface, both average fiber diameter is remeasured separately.

[0018] In addition, a filter element consists of one layer of the fiber cloth layer which consists of a nonwoven fabric or textile fabrics, or two or more layers, and each average fiber diameter of this fiber cloth layer is the same fiber cloth structure here as substantially as the average fiber diameter of this whole two or more fiber cloth layer.

[0019] moreover -- the case where it is filled up with the filter ingredient of this invention which consists of a nonwoven fabric and textile fabrics in a container, and it is used as a leukopheresis filter system -- the pack density of a nonwoven fabric or textile fabrics -- 0.1-0.4g/cm3 it is -- things -- desirable -- 0.15 - 0.38 g/cm3 it is -- things are more desirable. 0.1 g/cm3 Since there is a possibility of in the following deforming in case mechanical strengths run short and blood is made filtering, it is 0.4 g/cm3 preferably. When it exceeds, the repulsive force of a nonwoven fabric or textile fabrics is too high, and since it becomes difficult to be filled up in a container, it is not desirable. In addition, the pack density of a nonwoven fabric or textile fabrics is the value which broke by (effective filtration cross-section x thickness) of a nonwoven fabric the weight of the nonwoven fabric about the effective filtration cross-section part in the condition of having been dedicated in the container, or textile fabrics here.

[0020] Moreover, if the example of the giant-molecule porous body which can be suitably used in this invention is given, they will be a polyvinyl formal, a polyacrylonitrile, polysulfone, a cellulose, cellulose acetate, polyurethane, a polyvinyl acetal, polyester, a polyamide, Pori (meta) acrylate, etc. It is desirable that an average pore diameter is 1-60 micrometers, as for a macromolecule porous body, it is more desirable that it is 1-30 micrometers, and it is more desirable that it is further 1-20 micrometers. Since a possibility that the effectiveness of this invention may not fully be demonstrated since the contact probability of a porous body and a leucocyte is too low when 60 micrometers is exceeded conversely preferably, since there is a possibility that passage of an erythrocyte may become difficult, in less than 1 micrometer becomes strong, it is not desirable.

[0021] Moreover, as for the voidage of a macromolecule porous body, it is desirable that it is 45 - 95%, it is more desirable, and is more desirable. [further 80 - 95% of] [70 - 95% of] At less than 45%, since there is an inclination for mechanical strengths to run short when there is a possibility that the space which passes an erythrocyte cannot fully be offered and 95% is exceeded conversely, it is not desirable.

[0022] Moreover, even if the acid functional group of this invention is an acid functional group which the macromolecule itself which constitutes a filter ingredient has Moreover, the low-molecular object which has an acid functional group into the filter ingredient which originally does not have an acid functional group, A high polymer etc. may be introduced by fixing using all well-known approaches, such as precipitate insolubilization to covalent bond, ionic bond, physical adsorption, embedding, or an ingredient front face. Although alkali hydrolysis of the filter ingredient which consists of an ester compound, or the thing which fixed the ester compound may be carried out and an acid functional group may be produced, moreover, by the radiation graft or the plasma graft Since it can manufacture comparatively simple preferably since the improvement effect of the leukocyte-removal-capability force has the approach of carrying out the graft polymerization of the monomer which has an acid functional group, and going, and the high approach of coating the front face of the charge of a filter material with the polymer containing an acid functional group, and it excels also in the stability of the engine performance, it is desirable. In addition, in carrying out coating, in order to prevent omission from the charge of a filter material, it is desirable to construct a bridge in a polymer after coating.

[0023] If the example of the matter which has an acid functional group fixable [with such desirable technique] on a filter ingredient front face is given, as matter fixable [with graft polymerization] An acrylic acid, methacrylic acid, 2-methacryloiloxy-ethyl succinic acid, Monochrome (2-methacryloiloxy-ethyl) acid phosphate, The derivative of acrylic acids, such as 2-sulfoethyl methacrylate, or methacrylic acid, Although it is various kinds of vinyl monomers, such as allyl compounds, such as phenol derivatives, such as styrene derivatives, such as p-styrene sulfonic-acid sodium, and a vinyl phenol, and sodium allylsulfonate, an acetylene derivative, a trioxane derivative, etc. Especially a vinyl monomer has high polymerization nature, and since acquisition of a monomer is also comparatively easy, it is desirable. Moreover, there are a high molecular compound obtained by carrying out the polymerization of the above-mentioned monomer as matter fixable [with coating], a high molecular compound obtained as a copolymer of these monomers, and a polymerization nature functional group and the neutral monomer which has a vinyl group or an acetylenic group preferably further.

[0024] the consistency of the acid functional group of the ingredient in this invention -- per surface area of a filter ingredient, and 0.05 - 5 meq/m2 it is -- things -- desirable -- 0.08 - 1 meq/m2 it is -- things -- more -- desirable -- further 0.1 - 0.5 meq/m2 It is more desirable. 0.05 meq/m2 In the following, depending on the class of

functional group Since sufficient effectiveness may not be acquired, it is not desirable, and they are 5 meq/m2. If it exceeds When introducing a functional group into the front face of a nonwoven fabric, textile fabrics, and a macromolecule porous body by approaches, such as a radiation graft and polymer coating, amounts, such as a polymer introduced into the ingredient front face, are excessive. The opening of a filter ingredient is taken up, and since there is a possibility of checking remarkably the flow of the blood product which it is going to process, it is not desirable.

[0025] In this invention, although a good result will be obtained if it is an acid functional group, it is desirable that underwater Pka(s) are 1-6.5, and it is more desirable that it is 1-5.5. Moreover, if the desirable example of an acid functional group is given, they will be a carboxyl group, a phosphate group, a sulfonic group, a phenolic group, etc.

[0026] There are many unknown points about that there is effectiveness which raises leukocyte removal capability why in an acid functional group existing in a filter ingredient front face, electrostatic repulsive force works between the cell which originally has negative charge under physiological conditions, and the acid functional group which similarly has negative charge under physiological conditions -- although it comes out, the protein of a certain kind contained in plasma adsorbs early, and it is thought that adsorption of a leucocyte will therefore be promoted by agency of this protein rather than ****** probably sticks to this ingredient front face. In addition, the filter ingredient of this invention can be suitably used also as a filter ingredient for extracorporeal circulation mold leukopheresis therapies performed for the purpose of the therapy of a collagen disease, leukemia, etc.

[0027] In addition, it sets to this invention and whole blood 1 unit is 400-500ml (the blood volume specified in whole blood 1 unit changes with countries). In Japan, in 400ml and Germany, into the blood of being 450ml in 500ml, the United States, and France which collected blood For example, CPD, What carried out initial-complement addition of the anticoagulants, such as CPDA and ACD, is said. With erythrocyte pharmaceutical preparation 1 unit What added erythrocyte preservatives, such as Adsol, Neutricel, SAGM, and MAP, to the erythrocyte strong solution which removed and prepared some plasma or platelet rich plasma, and a buffy coat from whole blood 1 unit, and the erythrocyte strong solution is said.

[0028]

[Effect of the Invention] If leukopheresis in whole blood or erythrocyte pharmaceutical preparation is performed using the filter ingredient for the leukopheresis of this invention, it can compare with a filter ingredient without an acid functional group, a

leucocyte can be removed more to altitude, and a lower leucocyte survival rate can be attained about the blood after filtration.

[0029]

[Example] Next, an example is given and this invention is explained more to a detail.

[Example 1] In addition, the polymerization solution was adjusted so that it might become 2% (% of the weight) of concentration in water (vol/vol) about monochrome (2-methacryloiloxy-ethyl) acid phosphate 30% ethanol / 70%. the gamma ray which dips a polyester nonwoven fabric with an average fiber diameter of 1.7 micrometers created by the melt blowing method in this polymerization solution, performs nitrogen bubbling, seals after carrying out the nitrogen purge of the dissolved gas in a polymerization solution, and makes Co60 a line source — 2kGy exposure — carrying out — a radiation graft pile — therefore, the polymer of the above-mentioned monomer was lawfully introduced into the nonwoven fabric front face. After an exposure was completed, the nonwoven fabric was washed in 30-degree C warm water for 2 hours, and was dried by 40-degree C warm air overnight.

[0030] The quantum of the surface acidity functional group of this nonwoven fabric was performed by the following approach. 0.3g of nonwoven fabrics was cut finely, ethanol 4ml was added, and it was left for 1 hour, and after removing ethanol, 30ml of sodium chloride water solutions was added 4%, and it stirred for 12 hours. 15ml of solutions after removing a nonwoven fabric was weighed precisely, this was titrated with 0.01-N sodium-hydroxide water solution, and the amount of an acid functional group was measured from this point of neutralization. The surface acidity functional-group consistency of a nonwoven fabric was computed from this value and the specific-surface-area value of the nonwoven fabric measured using the BET adsorption method. consequently, the surface acidity functional-group consistency of this nonwoven fabric — 0.096 meq/m2 it was . effective so that it may become 0.20g [/cm] pack density 3 and thickness of 4.0mm about this nonwoven fabric — the filtration cross-section 30mmx30mm container was filled up, and the leukopheresis filter was created.

[0031] From 523ml of whole blood which added and prepared 63ml CPD into 450ml blood 243ml of platelet rich plasma is removed and prepared according to centrifugal separation within 8 hours after blood collecting. After leaving the erythrocyte pharmaceutical preparation (hematocrit 68%) saved for 19 days at 4 degrees C in a room temperature (26 degrees C) until it becomes 25 degrees C, The average fiber diameter of 32 micrometers and the 13-micrometer nonwoven fabric which were manufactured by the span bond method so that it may become average pack density

0.28 g/cm3 and the thickness of 3.5mm It moved to a blood bag effectively, new [about 60ml of these erythrocyte pharmaceutical preparation] after processing with the created pre-filter which filled up the filtration cross-section 67mmx67mm container with and removing a minute aggregate, and filtered with the above-mentioned filter.

[0032] After connecting a filter to the blood bag in which erythrocyte pharmaceutical preparation is contained through blood circuits in starting filtration, the blood bag has been held by hand, and was pressurized and blood was compulsorily filled in the filter. After blood was filled in the filter in this way, it passed continuously using the peristaltic pump by the fixed 2ml rate of flow for /, when the blood in a blood bag was exhausted, filtration was ended, the recovery bag connected to the filter lower stream of a river through blood circuits was cut the whole circuit in the place of 30-40cm of lower streams of rivers of the blood outlet of a filter, and erythrocyte pharmaceutical preparation in a circuit and a recovery bag was used as recovery liquid.

[0033] The erythrocyte pharmaceutical preparation before filtration (henceforth the liquid before filtration) and the volume of recovery liquid, and a white blood cell count were measured, and the leucocyte survival rate was searched for.

Leucocyte survival rate = {a white blood cell count (recovery liquid)} /{front [filtration] liquid product x leucocyte concentration (front [filtration] liquid)}

In addition, the volume of front [filtration] liquid and recovery liquid was made into the value which broke each weight by specific gravity 1.075. Moreover, measurement of the leucocyte concentration of the liquid before filtration was performed by the following approach. Measurement of the leucocyte concentration of the liquid before filtration: Pour into the counting chamber of a barker CHURUKU mold the liquid before filtration diluted 10 times with Turk solution, count the leucocyte which exists during large partition 4 partition using an optical microscope, and it is npre about this value. It carried out.

Leucocyte concentration =npre x(1/4) x105 An individual/ml [0034] Moreover, measurement of the white blood cell count of recovery liquid was described below, and it reached to an extreme of it, and it was based on the approach of high sensitivity. Into the bag containing recovery liquid, carrying out shaking mixing of recovery liquid and this capacity for the EBSS solution (henceforth ficoll liquid) of ficoll 400DL 5%, in addition, on the plasma skimming stand, it fixed and the recovery bag was put for 40 minutes. After collecting supernatants calmly so that the erythrocyte layer which is sedimenting may not be disturbed after standing, ficoll was again added to last time and this capacity recovery liquid bag, and the same actuation was repeated.

Centrifugal [of the supernatant collected by two actuation] was poured distributively and carried out to the Corning 25350 centrifugal tube for 840x g or 15 minutes, and the supernatant was discarded with the aspirator, warning against sucking up sediment. The supernatant was discarded with the aspirator, having added 200ml laked blood (1.145% oxalic acid ammonium physiological salt solution) to each centrifugal tube, having carried out shaking mixing, having carried out the at-long-intervals alignment immediately for 468x g or 10 minutes, and paying the same attention as all **.

[0035] After having brought sediment together in the 15ml centrifugal tube, adding laked blood and setting the whole quantity to 15ml, it put on the room temperature gently for 10 minutes, and the at-long-intervals alignment was carried out for 10 minutes, it left 468xg and 0.5ml containing sediment, and the supernatant was discarded carefully. After fully stirring the liquid containing sediment and considering as single cell suspension, 50micro (69.9mg / 1 bitter-taste chestnut gin orange liquid) of fluorescent stains I was added, and it stirred further. this liquid -- advanced NOIPA -- a well -- it poured into six formula counting chambers, and the leucocyte which exists during large partition 108 partition using an incident light type fluorescence microscope was counted. By the degree type, the white blood cell count (recovery liquid) was computed from this counted value npost.

White blood cell count (recovery liquid) = npostx(1/108) x104 x0.55x (1/0)
55)

[0036] It is the leucocyte concentration (a piece/ml) in the liquid (henceforth concentration liquid) finally condensed from recovery liquid to 0.55ml using ficoll liquid, and the underline section computes a white blood cell count by multiplying this by volume of 0.55ml of concentration liquid. Because the recovery at the time of collecting leucocytes using ficoll liquid is 55%, it divides by further 0.55. The leucocyte survival rate was 10-3.7 the following results.

[0037]

[The example 1 of a comparison] It experimented on the same conditions as an example 1 except having used the polyester nonwoven fabric with an average fiber diameter of 1.7 micrometers manufactured by the melt blowing method as it was (** which does not carry out a radiation graft). Consequently, the leucocyte survival rate was 10-2.6. In addition, as a result of measuring the surface acidity functional-group consistency of this nonwoven fabric, it was below limit of detection (0.05 meq/m2).

[0038]

[Example 2] Instead of monochrome (2-methacryloiloxy-ethyl) acid phosphate, it

experimented on the same conditions as an example 1 except having used 2-methacryloiloxy-ethyl succinic acid. Consequently, the leucocyte survival rate was 10-3.4. in addition, the result of having measured the surface acidity functional-group consistency of this nonwoven fabric -- 0.114 meq/m2 it was .

[0039]

[Example 3] Instead of monochrome (2-methacryloiloxy-ethyl) acid phosphate, in addition, it experimented on the same conditions as an example 1 except having adjusted the polymerization solution so that it might become 2% (% of the weight) of concentration 40% ethanol / 60% about 3 to 1 (mole ratio) mixture of a methacrylic acid and a methylmetaacrylate at water (vol/vol). Consequently, the leucocyte survival rate was 10-3.2. in addition, the result of having measured the surface acidity functional-group consistency of this nonwoven fabric -- 0.056 meq/m2 it was .

[0040]

[Example 4] Instead of monochrome (2-methacryloiloxy-ethyl) acid phosphate, in addition, it experimented on the same conditions as an example 1 except having adjusted the polymerization solution so that it might become 2% (% of the weight) of concentration 40% ethanol / 60% at water (vol/vol) about 3 to 1 (mole ratio) mixture of 2-methacryloiloxy-ethyl succinic acid and a methylmetaacrylate. Consequently, the leucocyte survival rate was 10-3.6. in addition, the result of having measured the surface acidity functional-group consistency of this nonwoven fabric -- 0.064 meq/m2 it was .

[0041]

[Example 5] Instead of monochrome (2-methacryloiloxy-ethyl) acid phosphate, in addition, it experimented on the same conditions as an example 1 except having adjusted the polymerization solution so that it might become 2% (% of the weight) of concentration 40% ethanol / 60% at water (vol/vol) about 3 to 1 (mole ratio) mixture of monochrome (2-methacryloiloxy-ethyl) acid phosphate and a methylmetaacrylate. Consequently, the leucocyte survival rate was 10-3.2. in addition, the result of having measured the surface acidity functional-group consistency of this nonwoven fabric -- 0.090 meq/m2 it was . The result of the above examples 1-5 and the example 1 of a comparison is collectively shown in Table 1.

[0042]

[Table 1]

	酸性官能基	表面酸性官能基密度	白血球残存率
実施例1	燐酸基	0.096meq/m^2	$10^{-3.7}$
実施例2	カルボキシル基	0.114meq/m^2	$10^{-3.4}$
実施例3	カルボキシル基	0.056meq/m^2	$10^{-3.2}$
実施例4	カルボキシル基	0.064meq/m^2	$10^{-3.6}$
実施例5	燐酸基	0.090meq/m^2	$10^{-3.2}$
比較例1	——	検出限界以下	$10^{-2.8}$

[0043]

[Example 6] p-styrene sulfonic-acid sodium was dissolved in the 5% 3rd class butanol / 95% water (vol/vol) so that it might become 2% (% of the weight) of concentration, and the polymerization solution was adjusted to it. the gamma ray which dips a polyester nonwoven fabric with an average fiber diameter of 1.7 micrometers created by the melt blowing method, and the polyester nonwoven fabric with an average fiber diameter of 1.2 micrometers similarly created by the melt blowing method in this polymerization solution, performs nitrogen bubbling, seals after carrying out the nitrogen purge of the dissolved gas in a polymerization solution, and makes Co60 a line source -- a 2.5kGy exposure -- carrying out -- a radiation graft pile -- therefore, the polymer of the above-mentioned monomer introduced into the nonwoven fabric front face lawfully. After an exposure was completed, the nonwoven fabric was washed in 30-degree C warm water for 2 hours, and was dried by 40-degree C warm air overnight.

[0044] The average fiber diameter of 32 micrometers and the 13-micrometer nonwoven fabric which were manufactured by the span bond method as a pre-filter so that it may become average pack density 0.28 g/cm3 and the thickness of 1.1mm A filtration cross-section 67mmx67mm container is filled up. effective -- as a main filter to the downstream in the same container A nonwoven fabric with an average fiber diameter [of a high order] of 1.7 micrometers Pack density 0.26 g/cm3, It was filled up so that it might become the thickness of 3.0mm, it was filled up with the nonwoven

fabric with a still more nearly same average fiber diameter [with the downstream / above-mentioned] of 1.2 micrometers so that it might become 0.32g [/cm] pack density 3 and thickness of 2.0mm, and the leukopheresis filter was created. After leaving the erythrocyte pharmaceutical preparation (hematocrit 55%) which added the physiological saline and was set to 360ml after removing and preparing 243ml of platelet rich plasma according to centrifugal separation within 8 hours after blood collecting from 523ml of whole blood which added and prepared 63ml CPD into 450ml blood and saving for three days at 4 degrees C in a room temperature (26 degrees C) until it became 25 degrees C, it was filtered with the above-mentioned filter. After connecting a filter to the blood bag in which erythrocyte pharmaceutical preparation is contained through blood circuits in starting filtration, the blood bag has been held by hand, and was pressurized and blood was compulsorily filled in the filter. After blood was filled in the filter in this way, when the blood in a sink and a blood bag was exhausted in blood by 1.5m of fall, filtration was ended, the recovery bag connected to the filter lower stream of a river through blood circuits was cut the whole circuit in the place of 30-40cm of lower streams of rivers of the blood outlet of a filter, and erythrocyte pharmaceutical preparation in a circuit and a recovery bag was used as recovery liquid. The leucocyte survival rate was searched for by the same approach as an example 1. Consequently, the leucocyte survival rate was 10-6.0.

[0045] In addition, the 0.01-N hydrochloric acid was used instead of the sodium chloride 4%, the solution after removing a nonwoven fabric was titrated in 0.01-N sodium-hydroxide water solution, the amount of the hydrochloric acid which decreased in number from this point of neutralization was calculated, and the surface acidity functional-group consistency of this nonwoven fabric was measured by the same approach as an example 1 except having made this amount into the amount of an acid functional group. consequently, a nonwoven fabric with an average fiber diameter of 1.7 micrometers — a nonwoven fabric with a 0.243 meq/m [2] and an average fiber diameter of 1.2 micrometers -- 0.291 meq/m2 it was .

[0046]

[The example 2 of a comparison] It experimented on the same conditions as an example 6 except having used the polyester nonwoven fabric with an average fiber diameter of 1.7 micrometers which omits radiation graft processing, and the polyester nonwoven fabric with an average fiber diameter of 1.2 micrometers as a main filter. Consequently, the leucocyte survival rate was 10-4.5. In addition, as a result of measuring the surface acidity functional-group consistency of this nonwoven fabric, it was below limit of detection (0.05 meq/m2).

[0047]

[Example 7] In addition, the whole quantity was set to 250ml so that it might become a water (vol/vol) solution about 2-methacryloiloxy-ethyl succinic acid 90% ethanol / 10% and might become the concentration of 0.25mol/1 about 0.75 mols/1 and a methylmetaacrylate. After carrying out the polymerization of V-65 at 45 degrees C under nitrogen-gas-atmosphere mind [so that it may become the concentration of 0.02mol/1] for 3 hours as a radical initiator, the matter which trickled into distilled water and has deposited was collected, it freeze-dried and the copolymer of 2-methacryloiloxy-ethyl succinic acid and a methylmetaacrylate was obtained. The average fiber diameter of 32 micrometers and the 13-micrometer nonwoven fabric which were manufactured by the span bond method as a pre-filter In average pack density 0.4 g/cm3 and thickness of 0.7 micrometers, moreover, a nonwoven fabric with an average diameter of 4.1 micrometers manufactured by the nonwoven fabric with an average fiber diameter of 12 micrometers and the milling-paper method which were manufactured by the air lei method So that it may become average pack density 0.30 g/cm3 and the thickness of 0.5mm A filtration cross-section 90mmx90mm container is filled up. effective -- as a main filter to the downstream in the same container A polyester nonwoven fabric with an average fiber diameter of 1.7 micrometers manufactured by the melt blowing method It is filled up so that it may become 0.38g [/cm] pack density 3 and thickness of 0.7mm. Furthermore, a polyester nonwoven fabric with an average fiber diameter of 1.2 micrometers manufactured by the melt blowing method as well as the downstream After being filled up so that it may become pack density 0.38 g/cm3 and the thickness of 2.5mm, The above-mentioned copolymer in a water (vol/vol) solution 90% ethanol / 10% By continuing passing nitrogen gas for 10 minutes, and carrying out a vacuum drying at a room temperature further overnight, after filling up the above-mentioned container with the copolymer solution which dissolved so that it might become the concentration of 0.05 g/dl and driving out a copolymer solution with nitrogen gas subsequently The above-mentioned copolymer was coated and the leukopheresis filter was created.

[0048] From 456ml of whole blood which added and prepared 56ml CPD into 400ml blood, 200ml of platelet rich plasma was removed and prepared according to centrifugal separation within 8 hours after blood collecting, and after leaving the erythrocyte strong solution (hematocrit 67%) saved for 14 days at 4 degrees C in a room temperature (26 degrees C) until it became 25 degrees C, this erythrocyte strong-solution 2 unit was brought together in the 600ml blood bag, and it filtered with the above-mentioned filter. It experimented by the same approach as an example 6

except having filtered by 1.2m of fall. Consequently, the leucocyte survival rate was 10-5.6. in addition, the result of having measured the surface acidity functional-group consistency of this nonwoven fabric -- a nonwoven fabric with an average fiber diameter of 1.7 micrometers --- a nonwoven fabric with a 0.095 meq/m [2] and an average fiber diameter of 1.2 micrometers --- 0.152 meq/m2 it was .

[0049]

[The example 3 of a comparison] It experimented on the same conditions as an example 7 except having not performed coating of a copolymer. Consequently, the leucocyte survival rate was 10-4.5. In addition, as a result of measuring the surface acidity functional-group consistency of this nonwoven fabric, it was below limit of detection (0.05 meq/m2).